```
  1 CAGCTCTCAT TTCTCCAAAA ATGTGTTTGA GCCACTTGGA AAATATGCCT
    GTCGAGAGTA AAGAGGTTTT TACACAAACT CGGTGAACCT TTTATACGGA
  1                       MetCysLeuS erHisLeuGl uAsnMetPro

 51 TTAAGCCATT CAAGAAGTCA AGGAGCTCAG AGATCATCCT GGAAGCTGTG
    AATTCGGTAA GTTCTTGAGT TCCTCGAGTC TCTAGTAGGA CCTTCGACAC
    LeuSerHisS erArgThrGl nGlyAlaGln ArgSerSerT rpLysLeuTrp

101 GCTCTTTTGC TCAATAGTTA TGTTGCTATT TCTTTGCTCC TTCAGTTGGC
    CGAGAAAACG AGTTATCAAT ACAACGATAA AGAAACGAGG AAGTCAACCG
 28  LeuPheCys SerIleValM etLeuLeuPh eLeuCysSer PheSerTrpL

151 TAATCTTTAT TTTTCTCCAA TTAGAGACTG CTAAGGAGCC CTGTATGGCT
    ATTAGAAATA AAAAGAGGTT AATCTCTGAC GATTCCTCGG GACATACCGA
    euIlePheIl ePheLeuGln LeuGluThrA laLysGluPr oCysMetAla

201 AAGTTTGGAC CATTACCCTC AAAATGGCAA ATGGCATCTT CTGAACCTCC
    TTCAAACCTG GTAATGGGAG TTTTACCGTT TACCGTAGAA GACTTGGAGG
 61 LysPheGlyP roLeuProSe rLysTrpGln MetAlaSerS erGluProPr

251 TTGCGTGAAT AAGGTGTCTG ACTGGAAGCT GGAGATACTT CAGAATGGCT
    AACGCACTTA TTCCACAGAC TGACCTTCGA CCTCTATGAA GTCTTACCGA
    oCysValAsn LysValSerA spTrpLysLe uGluIleLeu GlnAsnGlyLeu

301 TATATTTAAT TTATGGCCAA GTGGCTCCCA ATGCAAACTA CAATGATGTA
    ATATAAATTA AATACCGGTT CACCGAGGGT TACGTTTGAT GTTACTACAT
 95   TyrLeuIl eTyrGlyGln ValAlaProA snAlaAsnTy rAsnAspVal

351 GCTCCTTTTG AGGTGCGGCT GTATAAAAAC AAAGACATGA TACAAACTCT
    CGAGGAAAAC TCCACGCCGA CATATTTTTG TTTCTGTACT ATGTTTGAGA
    AlaProPheG luValArgLe uTyrLysAsn LysAspMetI leGlnThrLeu

401 AACAAACAAA TCTAAAATCC AAAATGTAGG AGGGACTTAT GAATTGCATG
    TTGTTTGTTT AGATTTTAGG TTTTACATCC TCCCTGAATA CTTAACGTAC
128  ThrAsnLys SerLysIleG lnAsnValGl yGlyThrTyr GluLeuHisV

451 TTGGGGACAC CATAGACTTG ATATTCAACT CTGAGCATCA GGTTCTAAAA
    AACCCCTGTG GTATCTGAAC TATAAGTTGA GACTCGTAGT CCAAGATTTT
    alGlyAspTh rIleAspLeu IlePheAsnS erGluHisGl nValLeuLys

501 AATAATACAT ACTGGGGTAT CATTTTACTA GCAAATCCCC AATTCATCTC
    TTATTATGTA TGACCCCATA GTAAAATGAT CGTTTAGGGG TTAAGTAGAG
161 AsnAsnThrT yrTrpGlyIl eIleLeuLeu AlaAsnProG lnPheIleSe

551 CTAGAGACTT GATTTGATCT CCTCATTCCC TTCAGCACAT GTAGAGGTGC
    GATCTCTGAA CTAAACTAGA GGAGTAAGGG AAGTCGTGTA CATCTCCACG
    rAM*
```

FIG. 1-1

```
 601 CAGTGGGTGG ATTGGAGGGA GAAGATATTC AATTTCTAGA GTTTGTCTGT
     GTCACCCACC TAACCTCCCT CTTCTATAAG TTAAAGATCT CAAACAGACA

 651 CTACAAAAAT CAACACAAAC AGAACTCCTC TGCACGTGAA TTTTCATCTA
     GATGTTTTTA GTTGTGTTTG TCTTGAGGAG ACGTGCACTT AAAAGTAGAT

 701 TCATGCCTAT CTGAAAGAGA CTCAGGGGAA GAGCCAAAGA CTTTTGGTTG
     AGTACGGATA GACTTTCTCT GAGTCCCCTT CTCGGTTTCT GAAAACCAAC

 751 GATCTGCAGA AATACTTCAT TAATCCATGA TAAAACAAAT ATGGATGACA
     CTAGACGTCT TTATGAAGTA ATTAGGTACT ATTTTGTTTA TACCTACTGT

 801 GAGGACATGT GCTTTTCAAA GAATCTTTAT CTAATTCTTG AATTCATGAG
     CTCCTGTACA CGAAAAGTTT CTTAGAAATA GATTAAGAAC TTAAGTACTC

 851 TGGAAAAATG GAGTTCTATT CCCATGGAAG ATTTACCTGG TATGCAAAAA
     ACCTTTTTAC CTCAAGATAA GGGTACCTTC TAAATGGACC ATACGTTTTT

 901 GGATCTGGGG CAGTAGCCTG GCTTTGTTCT CATATTCTTG GGCTGCTGTA
     CCTAGACCCC GTCATCGGAC CGAAACAAGA GTATAAGAAC CCGACGACAT

 951 ATTCATTCTT CTCATACTCC CATCTTCTGA GACCCTCCCA ATAAAAAGTA
     TAAGTAAGAA GAGTATGAGG GTAGAAGACT CTGGGAGGGT TATTTTTCAT

1001 GACTGATAGG ATGGCCACAG ATATGCCTAC CATACCCTAC TTTAGATATG
     CTGACTATCC TACCGGTGTC TATACGGATG GTATGGGATG AAATCTATAC

1051 GTGGTGTTAG AAGATAAAGA ACAATCTGAG AACTATTGGA ATAGAGGTAC
     CACCACAATC TTCTATTTCT TGTTAGACTC TTGATAACCT TATCTCCATG

1101 AAGTGGCATA AAATGGAATG TACGCTATCT GGAAATTTCT CTTGGTTTTA
     TTCACCGTAT TTTACCTTAC ATGCGATAGA CCTTTAAAGA GAACCAAAAT

1151 TCTTCCTCAG GATGCAGGGT GCTTTAAAAA GCCTTATCAA AGGAGTCATT
     AGAAGGAGTC CTACGTCCCA CGAAATTTTT CGGAATAGTT TCCTCAGTAA

1201 CCGAACCCTC ACGTAGAGCT TTGTGAGACC TTACTGTTGG TGTGTGTGTC
     GGCTTGGGAG TGCATCTCGA AACACTCTGG AATGACAACC ACACACACAG

1251 TAAACATTGC TAATTGTAAA GAAAGAGTAA CCATTAGTAA TCATTAGGTT
     ATTTGTAACG ATTAACATTT CTTTCTCATT GGTAATCATT AGTAATCCAA
```

FIG. 1-2

```
1301 TAACCCCAGA ATGGTATTAT CATTACTGGA TTATGTCATG TAATGATTTA
     ATTGGGGTCT TACCATAATA GTAATGACCT AATACAGTAC ATTACTAAAT

1351 GTATTTTTAG CTAGCTTTCC ACAGTTTGCA AAGTGCTTTC GTAAAACAGT
     CATAAAAATC GATCGAAAGG TGTCAAACGT TTCACGAAAG CATTTTGTCA

1401 TAGCAATTCT ATGAAGTTAA TTGGGCAGGC ATTTGGGGGA AAATTTTAGT
     ATCGTTAAGA TACTTCAATT AACCCGTCCG TAAACCCCCT TTTAAAATCA

1451 GATGAGAATG TGATAGCATA GCATAGCCAA CTTTCCTCAA CTCATAGGAC
     CTACTCTTAC ACTATCGTAT CGTATCGGTT GAAAGGAGTT GAGTATCCTG

1501 AAGTGACTAC AAGAGGCAAT GGGTAGTCCC CTGCATTGCA CTGTCTCAGC
     TTCACTGATG TTCTCCGTTA CCCATCAGGG GACGTAACGT GACAGAGTCG

1551 TTTAGAATTG TTATTTCTGC TATCGTGTTA TAAGACTCTA AAACTTAGCG
     AAATCTTAAC AATAAAGACG ATAGCACAAT ATTCTGAGAT TTTGAATCGC

1601 AATTCACTTT TCAGGAAGCA TATTCCCCTT TAGCCCAAGG TGAGCAGAGT
     TTAAGTGAAA AGTCCTTCGT ATAAGGGGAA ATCGGGTTCC ACTCGTCTCA

1651 GAAGCTACAA CAGATCTTTC CTTTACCAGC ACACTTTTTT TTTTTTTTCC
     CTTCGATGTT GTCTAGAAAG GAAATGGTCG TGTGAAAAAA AAAAAAAAGG

1701 TGCCTGAATC AGGGAGATCC AGGATGCTGT TCAGGCCAAA TCCCAACCAA
     ACGGACTTAG TCCCTCTAGG TCCTACGACA AGTCCGGTTT AGGGTTGGTT

1751 ATTCCCCTTT TCACTTTGCA GGGCCCATCT TAGTCAAATG TGCTAACTTC
     TAAGGGGAAA AGTGAAACGT CCCGGGTAGA ATCAGTTTAC ACGATTGAAG

1801 TAAAATAATA AATAGCACTA ATTCAAAATT TTTGGAATCT TAAATTAGCT
     ATTTTATTAT TTATCGTGAT TAAGTTTTAA AAACCTTAGA ATTTAATCGA

1851 ACTTGCNGGT TGCTTGTTGA AAGGNATATA ATGATTACAT TGTAAACAAA
     TGAACGNCCA ACGAACAACT TTCCNTATAT TACTAATGTA ACATTTGTTT

1901 TTTAAAATAT TTATGGATAT TTGTGAAAAG CTGCATTATG TTAAATAATA
     AAATTTTATA AATACCTATA AACACTTTTC GACGTAATAC AATTTATTAT

1951 TTACATGTAA AGCT
     AATGTACATT TCGA
```

FIG. 1-3

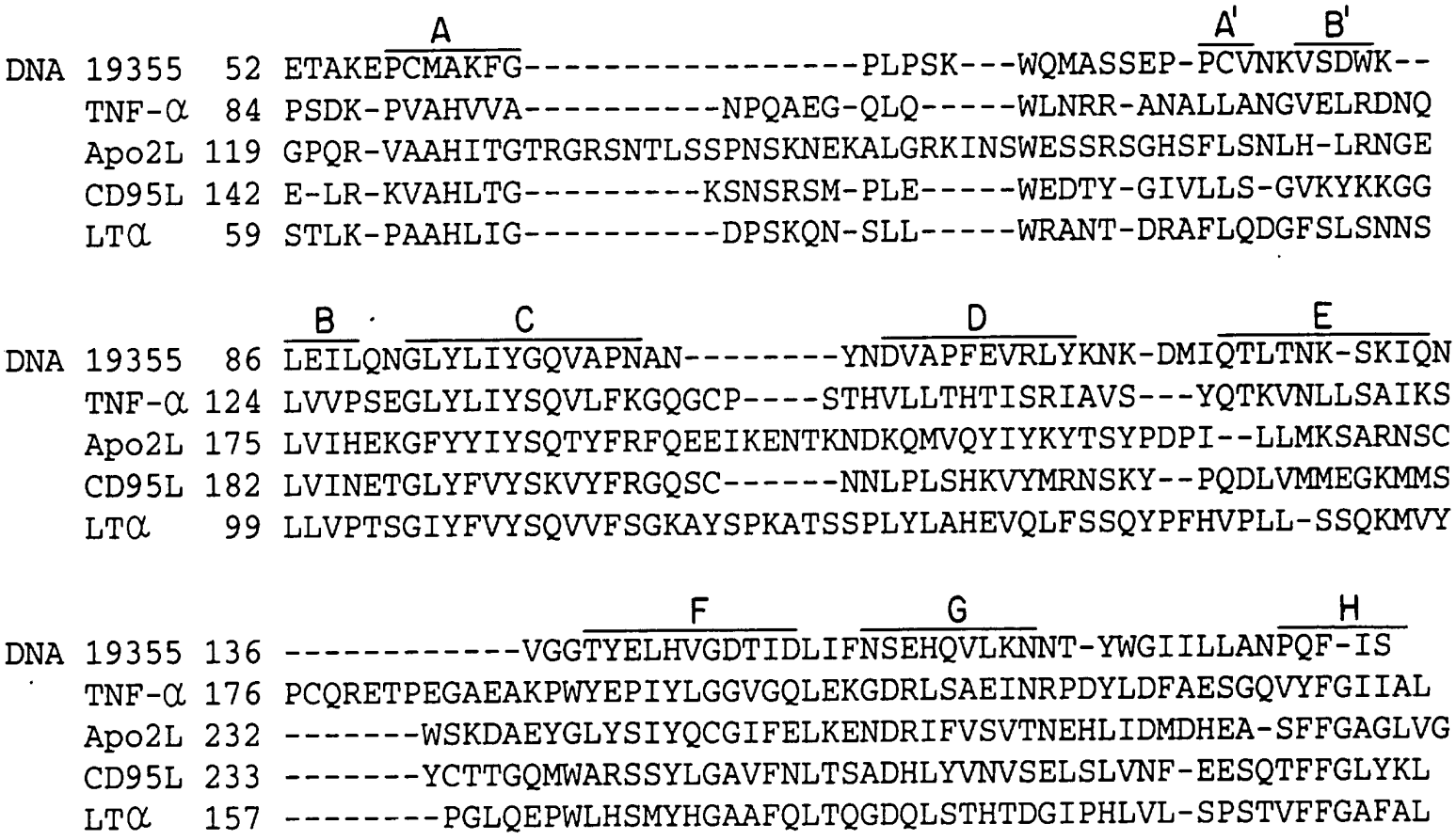
A
A'
B'
DNA 19355 52 ETAKEPCMAKFG----------PLPSK---WQMASSEP-PCVNKVSDWK--
TNF-α 84 PSDK-PVAHVVA----------NPQAEG-QLQ-----WLNRR-ANALLANGVELRDNQ
Apo2L 119 GPQR-VAAHITGTRGRSNTLSSPNSKNEKALGRKINSWESSRSGHSFLSNLH-LRNGE
CD95L 142 E-LR-KVAHLTG---------KSNSRSM-PLE-----WEDTY-GIVLLS-GVKYKKGG
LTα 59 STLK-PAAHLIG----------DPSKQN-SLL-----WRANT-DRAFLQDGFSLSNNS
B
C
D
E
DNA 19355 86 LEILQNGLYLIYGQVAPNAN--------YNDVAPFEVRLYKNK-DMIQTLTNK-SKIQN
TNF-α 124 LVVPSEGLYLIYSQVLFKGQGCP----STHVLLTHTISRIAVS---YQTKVNLLSAIKS
Apo2L 175 LVIHEKGFYYIYSQTYFRFQEEIKENTKNDKQMVQYIYKYTSYPDPI--LLMKSARNSC
CD95L 182 LVINETGLYFVYSKVYFRGQSC------NNLPLSHKVYMRNSKY--PQDLVMMEGKMMS
LTα 99 LLVPTSGIYFVYSQVVFSGKAYSPKATSSPLYLAHEVQLFSSQYPFHVPLL-SSQKMVY
F
G
H
DNA 19355 136 ------------VGGTYELHVGDTIDLIFNSEHQVLKNNT-YWGIILLANPQF-IS
TNF-α 176 PCQRETPEGAEAKPWYEPIYLGGVGQLEKGDRLSAEINRPDYLDFAESGQVYFGIIAL
Apo2L 232 -------WSKDAEYGLYSIYQCGIFELKENDRIFVSVTNEHLIDMDHEA-SFFGAGLVG
CD95L 233 -------YCTTGQMWARSSYLGAVFNLTSADHLYVNVSELSLVNF-EESQTFFGLYKL
LTα 157 --------PGLQEPWLHSMYHGAAFQLTQGDQLSTHTDGIPHLVL-SPSTVFFGAFAL

FIG. 2

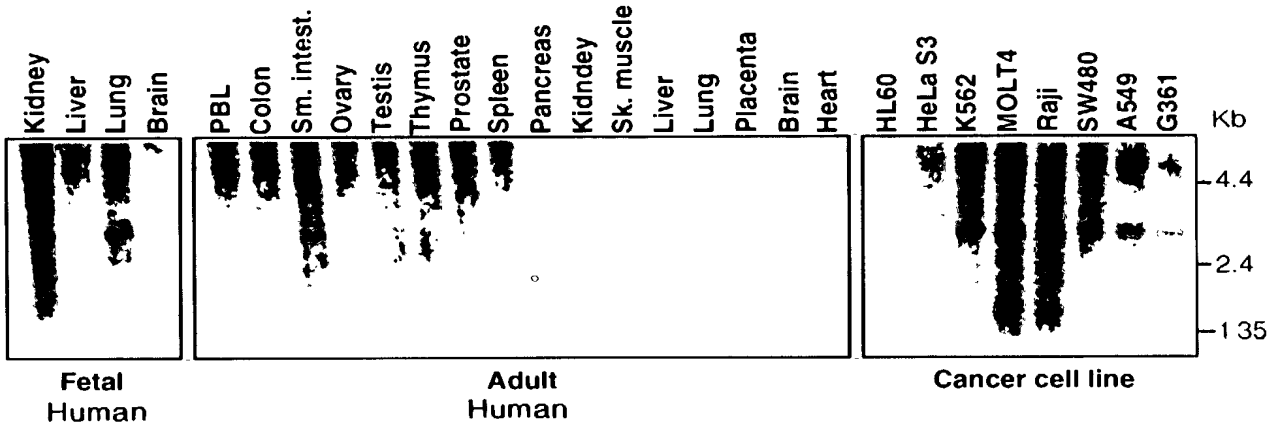
Kidney
Liver
Lung
Brain
PBL
Colon
Sm. intest.
Ovary
Testis
Thymus
Prostate
Spleen
Pancreas
Kidndey
Sk. muscle
Liver
Lung
Placenta
Brain
Heart
HL60
HeLa S3
K562
MOLT4
Raji
SW480
A549
G361
Kb
4.4
2.4
1.35
Fetal Human
Adult Human
Cancer cell line

FIG. 3

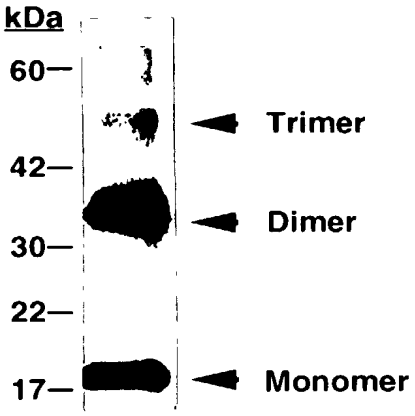
kDa
60
42
30
22
17
Trimer
Dimer
Monomer

FIG. 4

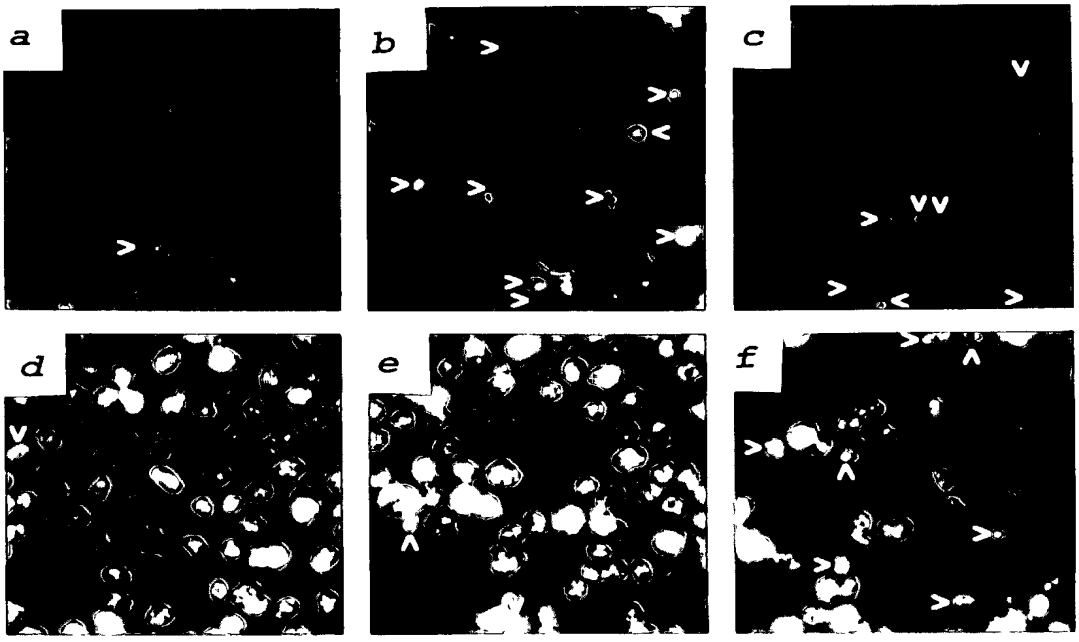

FIG. 5A

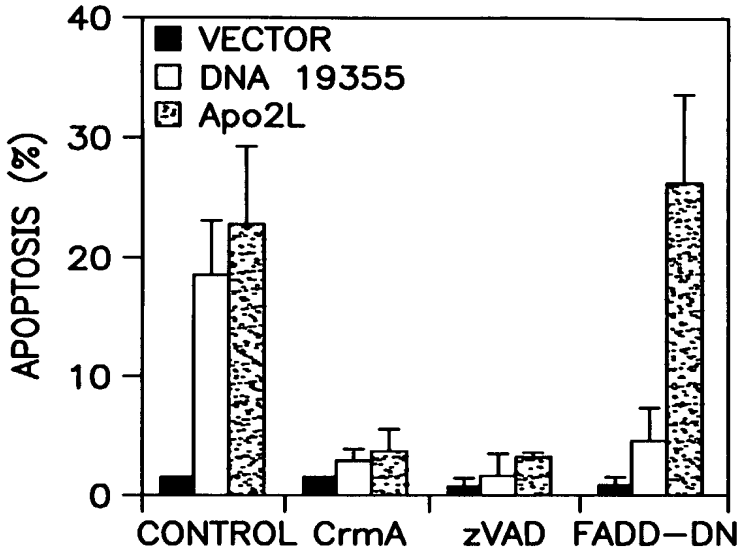
40
30
20
10
0
APOPTOSIS (%)
VECTOR
DNA 19355
Apo2L
CONTROL
CrmA
zVAD
FADD-DN

FIG. 5B

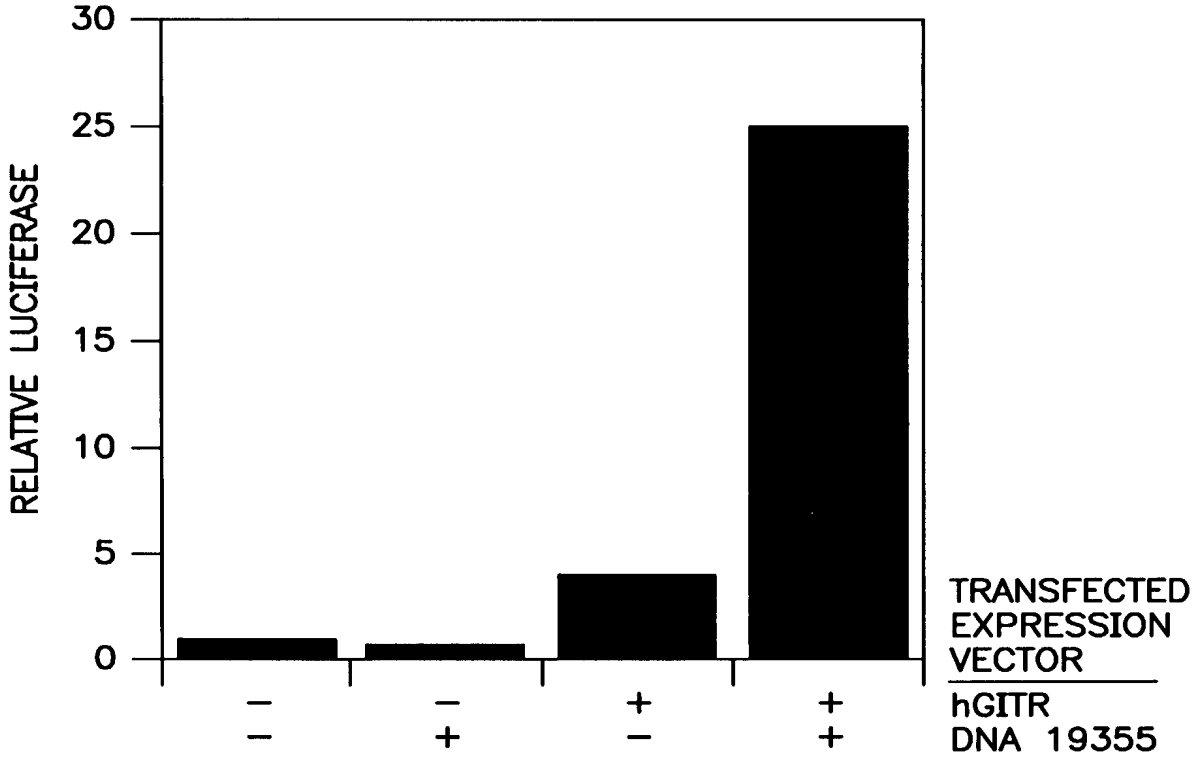
30
25
20
15
10
5
0
RELATIVE LUCIFERASE
TRANSFECTED
EXPRESSION
VECTOR
hGITR
DNA 19355
- - + +
- + - +

FIG. 10

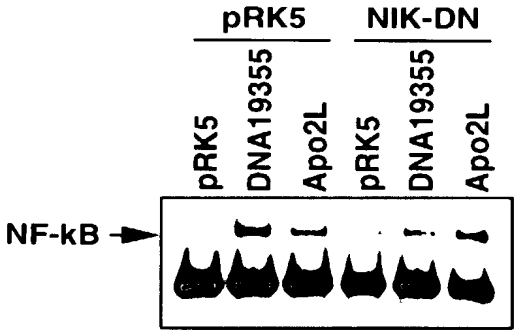
pRK5
NIK-DN
pRK5
DNA19355
Apo2L
pRK5
DNA19355
Apo2L
NF-kB

FIG. 6

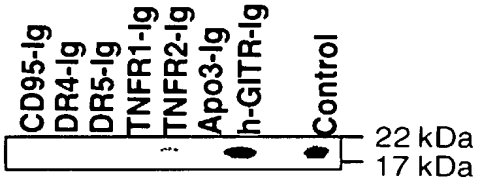
CD95-Ig
DR4-Ig
DR5-Ig
TNFR1-Ig
TNFR2-Ig
Apo3-Ig
h-GITR-Ig
Control
22 kDa
17 kDa

FIG. 8

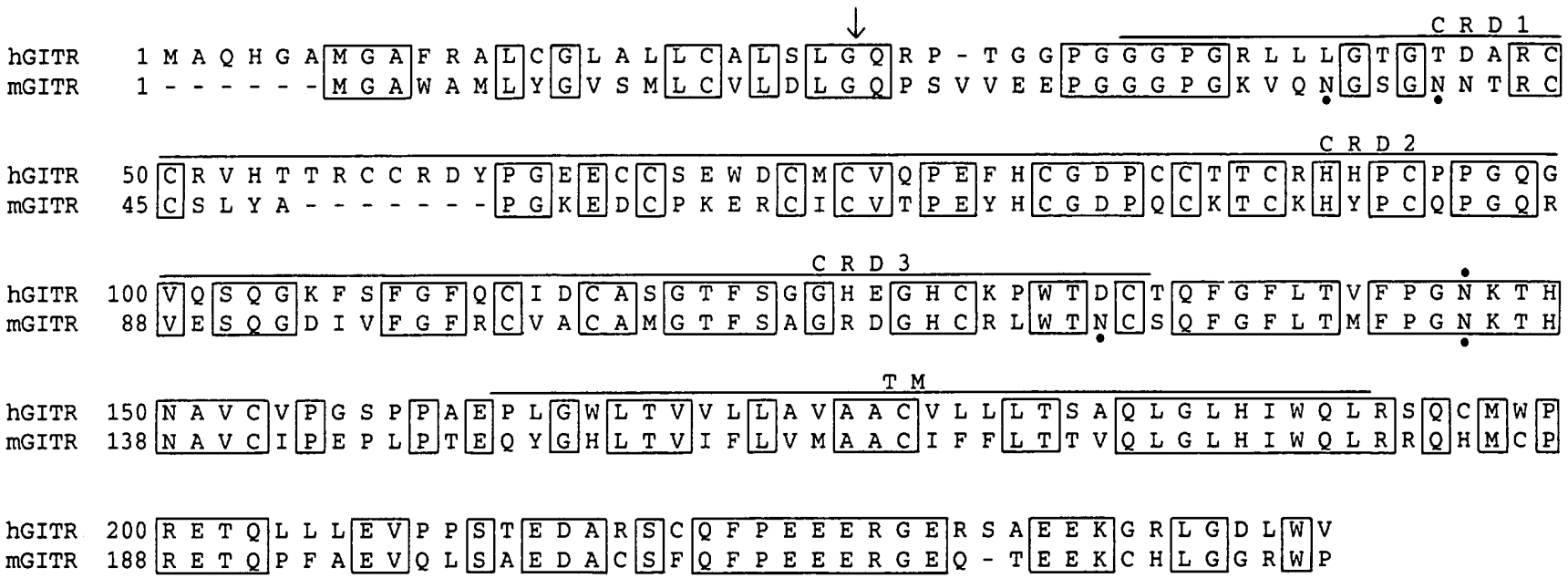
CRD1
CRD2
CRD3
TM
hGITR 1 MAQHGAMGAFRALCGLALLCALSLGQRP-TGGPGGGPGRLLLGTGTDARC
mGITR 1 ------MGAWAMLYGVSMLCVLDLGQPSVVEEPGGGPGKVQNGSGNNTRC
hGITR 50 CRVHTTRCCRDYPGEECCSEWDCMCVQPEFHCGDPCCTTCRHHPCPPGQG
mGITR 45 CSLYA-------PGKEDCPKERCICVTPEYHCGDPQCKTCKHYPCQPGQR
hGITR 100 VQSQGKFSFGFQCIDCASGTFSGGHEGHCKPWTDCTQFGFLTVFPGNKTH
mGITR 88 VESQGDIVFGFRCVACAMGTFSAGRDGHCRLWTNCSQFGFLTMFPGNKTH
hGITR 150 NAVCVPGSPPAEPLGWLTVVLLAVAACVLLLTSAQLGLHIWQLRSQCMWP
mGITR 138 NAVCIPEPLPTEQYGHLTVIFLVMAACIFFLTTVQLGLHIWQLRRQHMCP
hGITR 200 RETQLLLEVPPSTEDARSCQFPEEERGERSAEEKGRLGDLWV
mGITR 188 RETQPFAEVQLSAEDACSFQFPEEERGEQ-TEEKCHLGGRWP

FIG. 7

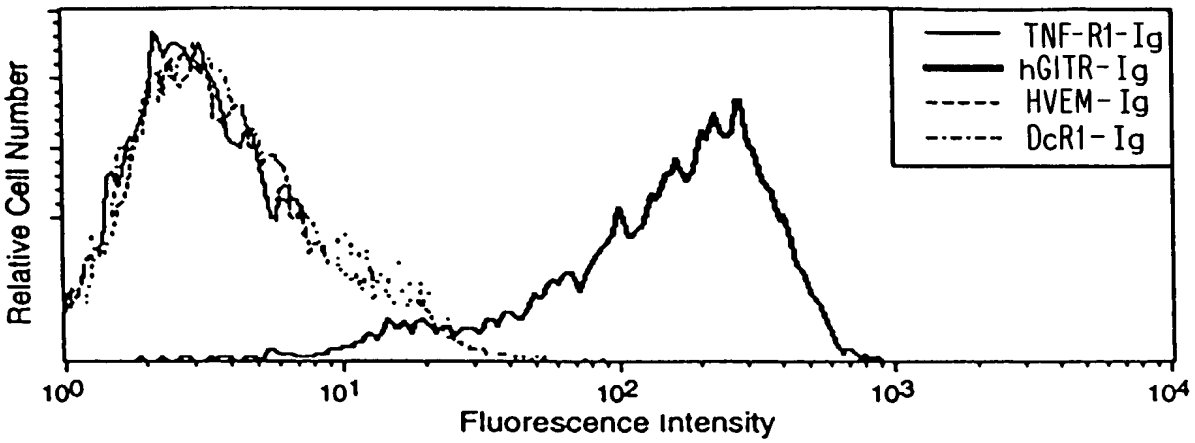
TNF-R1-Ig
hGITR-Ig
HVEM-Ig
DcR1-Ig
Relative Cell Number
10^0
10^1
10^2
10^3
10^4
Fluorescence Intensity

FIG. 9A

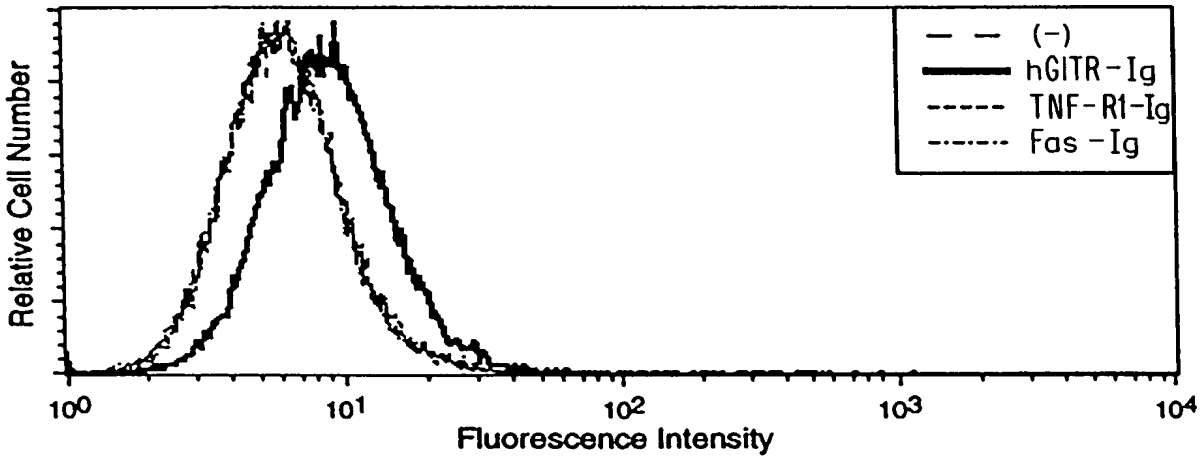
(-)
hGITR-Ig
TNF-R1-Ig
Fas -Ig
Relative Cell Number
10^0
10^1
10^2
10^3
10^4
Fluorescence Intensity

FIG. 9B

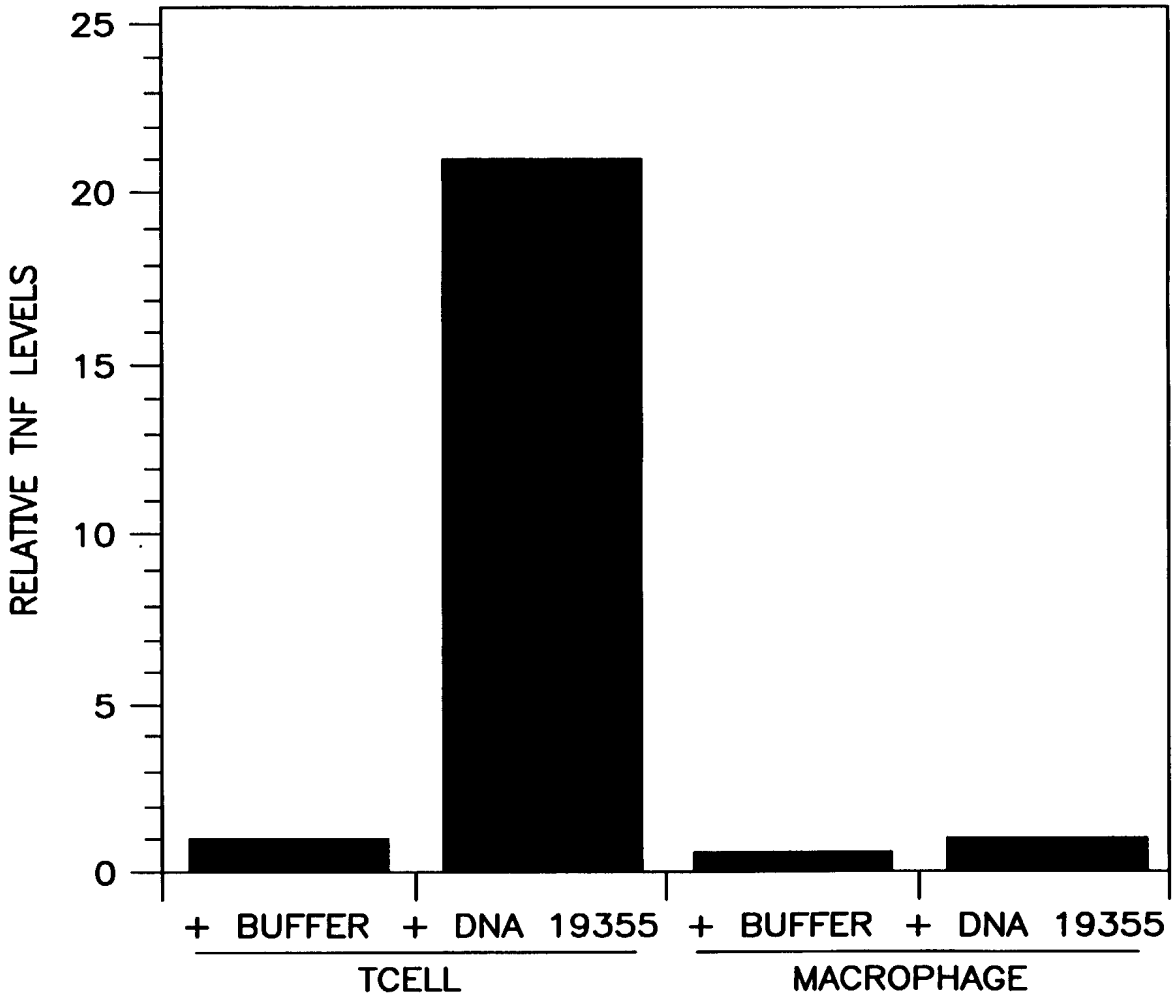
25
20
15
10
5
0
RELATIVE TNF LEVELS
+ BUFFER
+ DNA 19355
+ BUFFER
+ DNA 19355
TCELL
MACROPHAGE

FIG. 11